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*Research Article*

# Studies on Cohesiveness of Isolated Starch from the Seeds of *Cajanas Cajan*

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**Abstract**

The objective of the present investigation was to extract starch from the seeds of *Cajanas cajan* (*family Fabiaceae*) and to evaluate its cohesive properties as a binder in the formulation of tablets using Ranitidine hydrochloride as a model drug. *Cajanus cajan* seeds contain 20-21% of carbohydrate of which 60% of starch present was isolated by hot water extraction, maceration and subsequent non-aqueous solvent precipitation method.The micromeritic properties of isolated starch possessed bulk density of 0.58 g/cc with good flow properties and compressibility. The formulations of ranitidine hydrochloride with increased concentration of isolated starch 4-12% by weight of tablet were prepared by wet granulation technique. The IR spectral studies indicated good compatibility between the drug and the polymer. The results of weight variation and drug content indicated that all the formulated tablets were uniform with low standard deviation values. The binder concentrations had a positive influence on the hardness of the tablets. The formulation F-2 with binder 8 % w/w of tablet showed desired hardness, friability, disintegration and similar dissolution profile in concordant to the conventional marketed product. The comparative cohesiveness efficiency of the *Cajanas cajan* seed starch with other established binders potato starch, methyl cellulose and PVP were studied. It was observed that with 8% w/w of binder in the tablet, the methyl cellulose possessed highest hardness with delayed disintegration time. The drug release at the end of 40 min. was found to be complete with *Cajanas cajan* seed starch as compared with other binders used. Thus the extracted *Cajanas cajan* seed starch could be used as an alternative and effective natural polymer binder in the manufacture of tablets and its concentration can be optimized depending upon the physico-chemical, micromeritic properties of the drug and other excipients.

## 1. INTRODUCTION

The formulation of tablets require binder as one of the most important excipient which determines the cohesivity and hardness of the granules. Binding agents are used to impart the structural strength required during the processing, handling and packaging of tablets. The selection and optimum concentration of the binder in the tablet manufacture is very critical as it influences the disintegration rate of the tablet.

Polysaccharide hydrocolloids including mucilages, gums and glucans are abundant in nature and commonly found in many higher plants. These polysaccharides constitute a structurally diverse class of biological macromolecules with a broad range of various applications in pharmacy and medicine. Although plant organs, their physiological function in most cases is unclear, mucilages found in rhizomes, roots and seed endosperms may act as energy reserves primarily.[1] Pigeon pea also known as tropical green pea is obtained from a tropical cereal plant – *Cajanus cajan* L. Millisp., family Fabaceae, which is widely cultivated in more than 25 tropical and subtropical countries in Asia, Africa and Central America. Pigeon peas are food (dried peas, flour, or green vegetable peas) and forage/cover crop. In many of these countries, pigeon pea is consumed after boiling. They contain high levels of carbohydrate with protein and the important amino acids – methionine, lysine, and tryptophan. Pigeon pea flour contains 22.4% protein, 2.6% fat, 5.8% ash, 3.8% fiber and 59.4% carbohydrate. The starch content of pigeon pea contributes 29.7% on a whole seed basis and it exhibits a restricted two-stage swelling pattern and a moderate solubility in water.[2]

Ranitidine Hydrochloride is an $H_2$ blocker that is used to block the action of histamine on the parietal cells in the stomach, decreasing acid production in the stomach. The $H_2$ antagonists are competitive inhibitors of histamine at the parietal cell $H_2$ receptor and used for the treatment of peptic ulcers. They suppress the normal secretion of acid by the parietal cells and the meal-stimulated acid secretion.[3]

The present study aims at investigation of the binder effects of *Cajanus cajan* seed mucilage on the mechanical properties of tablet formulations using Ranitidine hydrochloride as a model drug and to compare the binding efficacy with established existing binders.

## 2. MATERIALS AND METHODS

### 2.1 Isolation and evaluation of starch from the seeds of *Cajanus cajan*

*2.1.1 Extraction of Mucilage*

The seeds of *Cajanus cajan* were collected, authenticated and powdered using a mill. The powder was then boiled and macerated using purified water for 30 minutes. The extract was then pressed through muslin cloth. The filtrate containing starch mucilage was then cooled to room temperature[4].

*2.1.2 Isolation of Mucilage*

To the filtrate, acetone was added in 1:2 proportions to precipitate out mucilage. The mucilage so obtained was then subjected to air drying for sufficient period of time and further dried in an oven at 45°C. The well dried starch mucilage was powdered with the help of mortar and pestle and passed through sieve #85 and stored in an air tight container until further use.[4]

*2.1.3 Physicochemical Characteristics of Mucilage*

The physicochemical characteristics of the isolated mucilage powder such as solubility, swelling index, loss on drying, bulk density, tap density, angle of repose, melting point were determined as per Pharmacopoeial procedures and pH of 1% solution was determined using digital pH meter[5].

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**2.2 Formulation of Ranitidine Hydrochloride Tablets using Isolated Starch as the Binder**

The formulations were prepared by wet granulation method using isolated starch of the concentration 4, 8, 10, 12%w/w of the tablet as the binder. The selected formulation was then compared for binder efficacy with the other established binder concentration.

The drug and excipients for the batch formulation of 50 tablets were weighed and individually passed through sieve # 44. Weighed quantity of the drug was mixed uniformly with lactose, binder and half the portion of sodium starch glycollate using a pestle and mortar. Sufficient quantity of luke warm water was added to the powder blend and mixed well to form a coherent mass. The dough mass was passed through sieve#12 and the granules obtained were dried at the temperature of $40^0$C. The dried granules were again passed through sieve#16 and lubricated with remaining portion of sodium starch glycollate, purified talc and magnesium stearate. The lubricated granules were subjected to pre-compression evaluation and compressed into tablets using single rotary tablet compression machine (RIMEK RSB-4 Minipress, Ahmedabad).

**2.3 Evaluation Studies**

*2.3.1 Pre-compression Studies*

*2.3.1.1 Drug: Polymer Compatibility Studies*

The drug and polymer compatibility studies were carried out using Fourier Transform Infrared spectrophotometer. The FT-IR was recorded individually for the extracted *Cajanus cajan* seed mucilage, ranitidine hydrochloride and physical mixture of 1:1 ratio drug: polymer. The sample was mixed with KBr in 1:1 ratio and the resulting powder was scanned using computer mediated Fourier transformed Infrared spectrophotometer (FTIR 8400 S, Shimadzu, Japan) [6].

*2.3.1.2 Angle of Repose*

The angle of repose of the granules was determined by fixed funnel method to assess the flow property of the granules. The diameter of the granules cone (d) and the height (h) of the pile were noted. From the diameter, radius (r) was calculated. The angle of repose (θ) was calculated using the following formula:

$$\theta = \tan^{-1} (h/r)$$

*2.3.1.3 Bulk Density*

An accurately weighed quantity of granules (W) was carefully transferred into 250 ml measuring cylinder and initial volume (V0) was measured. The bulk density was calculated using following formula. [7]

Bulk Density = Mass of the granules (W)/ Initial volume of granules (V0)

*2.3.1.4 Tapped Density*

An accurately weighed quantity of granules (W) was carefully transferred into 100 ml measuring cylinder. The cylinder was then fixed to the Tap density apparatus (Electrolab ETD 1020, Mumbai). USP II mode was selected and the apparatus was operated at 250 tappings /min. The measuring cylinder was tapped at the height of 1 cm. The tapping was continued until no further change in volume (until a constant volume) was obtained (Vf). The tapped density was calculated by the following formula. [8]

Tapped Density = Mass of the granules (W)/ Tapped volume of granules ($V_f$)

*2.3.1.5 Bulkiness*

Bulkiness is a reciprocal of bulk density. It is expressed by cc/gram[9]

*2.3.1.6 Compressibility Index and Hausner Ratio*

The compressibility index and the Hausner ratio were determined by equating both the bulk density and tapped density of the granules.

Compressibility Index = Tapped density / Bulk density X 100

Hausner Ratio = Tapped density / Bulk density

**2.4 Post-compression Studies**

*2.4.1 Hardness Test*

The mechanical strength of the batch tablets from each formulation was tested using Monsanto hardness tester[10].

*2.4.2 Friability Test*

The test was conducted using Roche Friabilator. Weighed tablets of 6.5g were loaded into the instrument and operated at 25rpm for 4 minutes. The tablets were taken out and weight of the dedusted tablets was recorded[10].

Friability = Initial weight – Final weight / Initial weight X 100

*2.4.3 Weight Variation Test*

For uniformity of weight determination, twenty tablets were randomly selected from each formulation and weighed using a digital balance. Average weight was determined and the tablets were individually weighed and deviation from the average weight was calculated[11].

*2.4.4 Disintegration Test*

The test was conducted by using USP Disintegration test apparatus by placing each tablet in each basket and the process was carried out using pH 7.4 phosphate buffer media maintained at $37^0$C.

*2.4.5 Drug Content*

Accurately weighed ten tablets from each formulation were triturated to fine powder. Tablet triturate equivalent to 150 mg of ranitidine hydrochloride was weighed and dissolved in sufficient quantity of 7.4 pH buffer and volume was made up. The solutions were suitably diluted with buffer and the content of the drug was estimated at 314 nm against buffer media pH 7.4 as the blank. using UV-Visible double beam spectrophotometer (UV-1601 Shimadzu, Japan).

*2.4.6 In-vitro Drug Release Study*

The dissolution studies were carried out using USP XXIII – Paddle type Dissolution test apparatus (LABINDIA DS 8000). The dissolution medium used was 900 ml of pH 7.4 buffer with controlled temperature of 37 + $0.5^0$C stirred at 50rpm. At predetermined time intervals, samples of known volume were withdrawn and replaced with fresh media to maintain the sink condition. Collected samples were suitably diluted with buffer and analyzed at 314 nm against buffer pH 7.4 as blank using UV Visible spectrophotometer (UV-1601 Shimadzu, Japan).

**3. RESULTS AND DISCUSSION**

The isolation of starch from the seeds of *Cajanus cajan* (family *fabiaceae)* by aqueous extraction and non-aqueous precipitation was successfully established. The isolated starch product had good bulk density of 0.588g/cc. and flow properties. To investigate the cohesive property of the isolated starch as a binder, ranitidine hydrochloride conventional tablets were prepared by wet granulation technique using different concentrations of binder ( 4-12% of tablet weight) and compared with other widely used binders. The IR spectral studies as indicated in the Figures 1-3 showed identical peaks of drug and polymer in the physical mixture when compared to the pure samples ascertaining the drug-polymer compatibility. The results of weight variation and drug content indicated in (Table 4) showed that all the formulated tablets were uniform with low standard deviation values. The hardness of the tablets increased with increase in the binder concentration. The disintegration time and dissolution profile of the formulation F-2 with binder concentration 8% w/w of tablet and marketed product were almost similar and thus selected for further comparative studies with other binder polymers. The values of hardness and the disintegration time were better when compared with the other binders. The drug release at the end of 40 min. was found to be in the order of: F-2 (98.4%), F-PVP (85%), F-MC (78%) and F-Starch (62%) respectively.

**Table 1:** Physical and derived properties of isolated starch mucilage

| | |
|---|---|
| Solubility | Partially soluble in chloroform and hot water. Insoluble in cold water, 0.1N HCl, 7.4pH phosphate buffer and acetone. |
| pH of 1% w/v solution | 6.2 |
| Loss on drying | 0.3560 % |
| Swelling index | 233.3 % |
| Bulk density | 0.5882 g/cc |
| Tapped density | 0.7692 g/cc |
| Melting point | 168-170ºC |
| Angle of repose | 22.68º |

**Table 2:** Composition of Ranitidine hydrochloride tablet formulations

| Ingredients | F-1 | F-2 | F-3 | F-4 | F- Starch | F- MC | F-PVP |
|---|---|---|---|---|---|---|---|
| Ranitidine (mg) | 150 | 150 | 150 | 150 | 150 | 150 | 150 |
| Anhydrous lactose (mg) | 74 | 64 | 54 | 44 | 64 | 64 | 64 |
| Sodium starch glycollate (mg) | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| Binding agent (%w/w of tablet) | 4%w/w (10mg) *Cajanas cajan* | 8%w/w (20mg) *Cajanas cajan* | 10%w/w (25mg) *Cajanas cajan* | 12%w/w (30mg) *Cajanas cajan* | 8%w/w (20mg) Potato starch | 8%w/w (20mg) Methyl cellulose | 8%w/w (20mg) Polyvinyl pyrrolidone |
| Purified talc (mg) | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| Magnesium stearate (mg) | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Tablet Weight (mg) | 250 | 250 | 250 | 250 | 250 | 250 | 250 |

Table 3: Pre compression studies of the tablet formulations

| Parameter | F1 | F2 | F3 | F4 |
|---|---|---|---|---|
| Bulk density (g/cc) | 0.407 | 0.4436 | 0.5036 | 0.4047 |
| Tap density (g/cc) | 0.4788 | 0.5268 | 0.6155 | 0.5000 |
| Carr's Index (%) | 14.99 | 18.77 | 22.22 | 19.20 |
| Hausner's Ratio | 1.1764 | 1.1875 | 1.2222 | 1.2376 |
| Bulkiness | 2.457 | 2.2542 | 1.9857 | 2.4750 |
| Angle of Repose (degrees) | 31.175 | 30.423 | 32.220 | 34.124 |

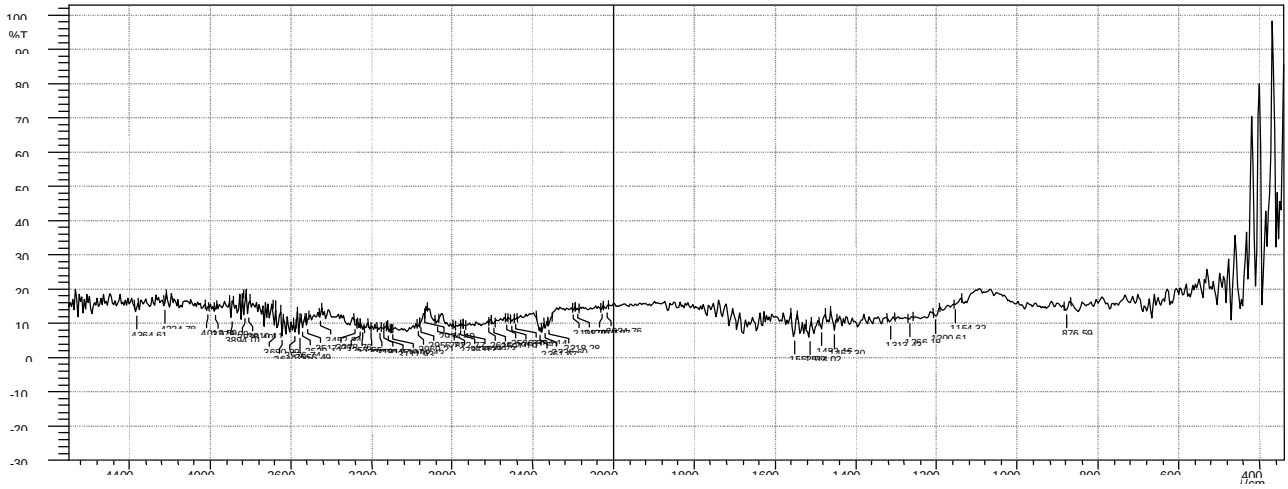


**Fig.1:** IR spectrum of *Cajanus* mucilage powder

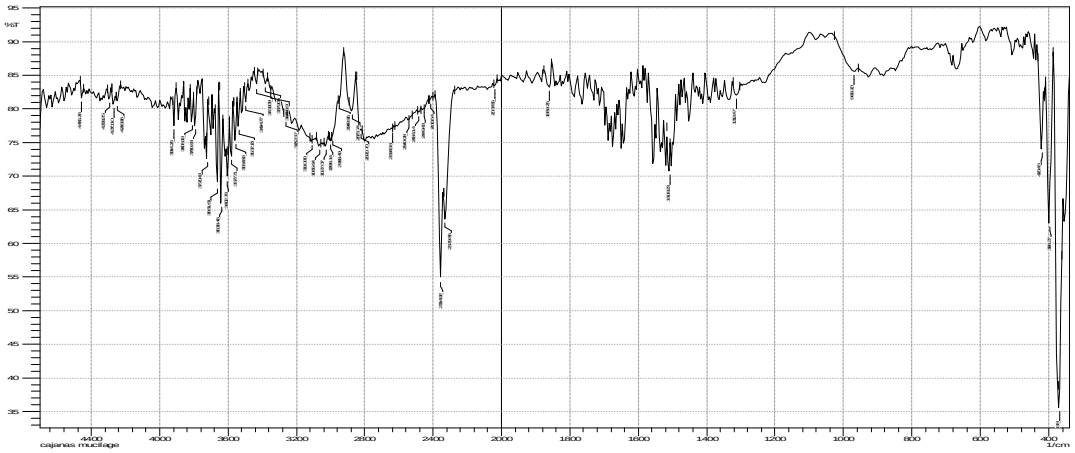

**Fig.2:** IR spectrum of Ranitidine hydrochlorid

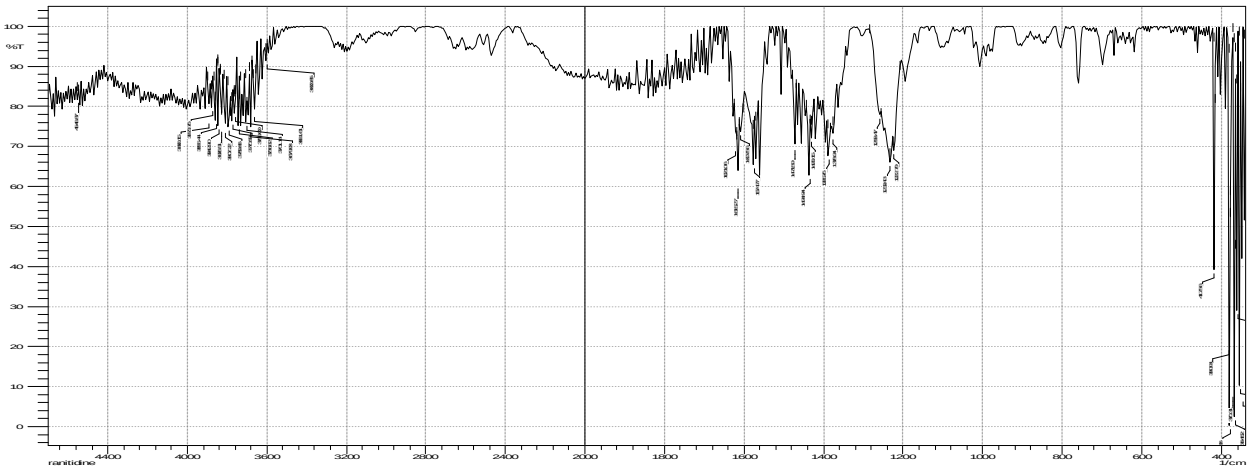

**Fig.3:** IR spectrum physical mixture of Ranitidine hydrochloride and *Cajanus cajan* seed mucilage

**Table 4:** Post compression studies of the tablet batch formulations

| Parameters | F-1 | F-2 | F-3 | F-4 | F-Starch | F-MC | F-PVP |
|---|---|---|---|---|---|---|---|
| Hardness* (Kg/cm$^2$) | 4.6±1.2 | 5.0±0.8 | 5.0±0.6 | 5.2±0.8 | 5.5±1.2 | 5.0±0.4 | 4.8±1.6 |
| Friability (%) | 0.36 | 0.22 | 0.34 | 0.22 | 0.34 | 0.28 | 0.27 |
| Disintegration time*(minutes) | 6.24±0.26 | 6.51±0.58 | 7.13±0.36 | 7.36±0.22 | 6.56±0.38 | 8.37±0.12 | 7.12±0.54 |
| Assay* (%) | 98.13±1.2 | 99.76±2.6 | 100.46±3.2 | 99.17±2.1 | 99.67±2.8 | 98.87±1.9 | 99.74±2.4 |

* Average of three determinations± S.D.

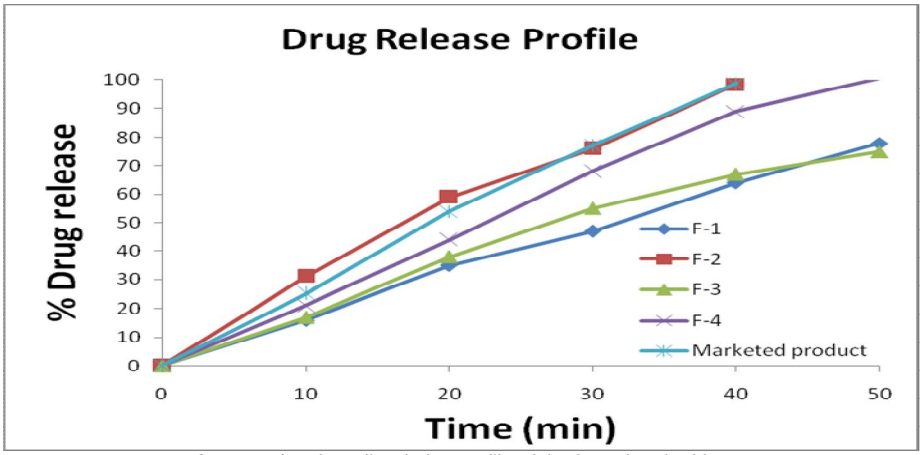


**Fig.4:** *In-vitro* drug dissolution profile of the formulated tablets

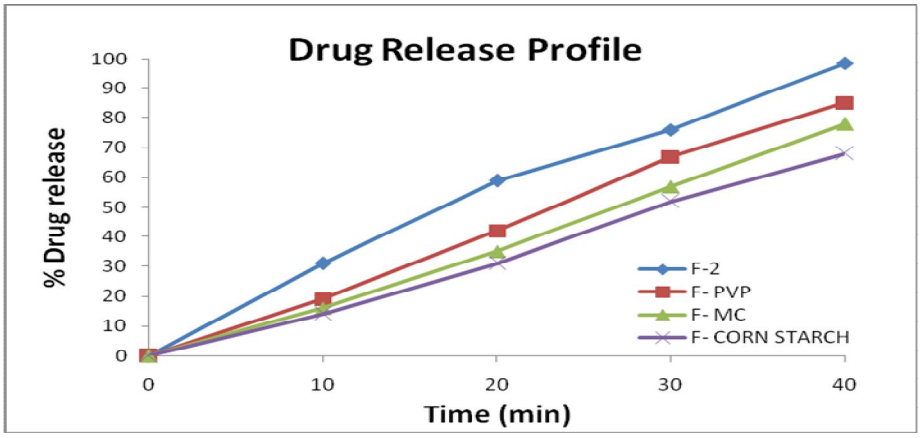


**Fig.5:** Comparative *in-vitro* drug dissolution profile with varied binders of the selected formulation

## 4. CONCLUSION

The tablet cohesive property of isolated starch from *Cajanus cajan* seed was investigated and reported to be a good granulating agent for the formulation of tablets. The tablets of ranitidine showed good mechanical strength with better disintegration and dissolution profile when compared with the existing selected binders. Thus depending upon the tablet strength and suitability of drug release requirement, the concentration of the *Cajanus cajan* seed starch binder could be optimized for the manufacture of various tablet dosage form.

## 5. ACKNOWLEDGEMENT

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